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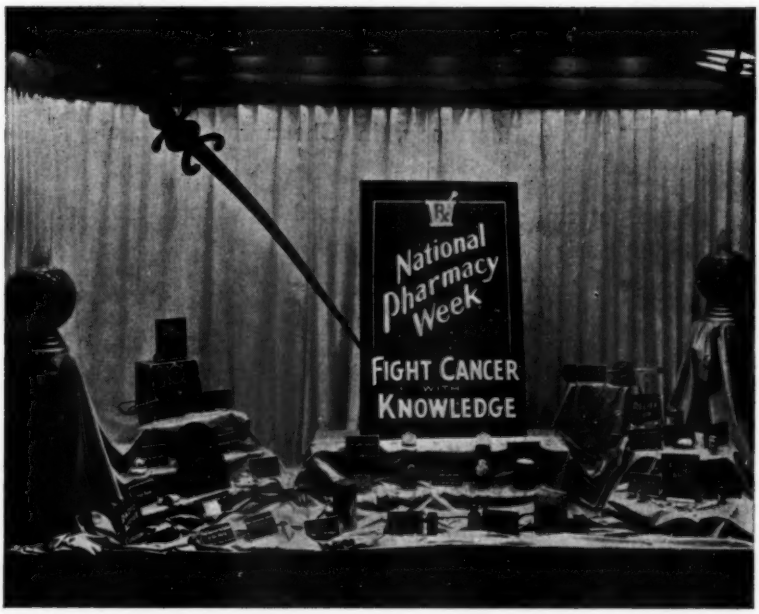

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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

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E D I T O R I A L

RACIAL AND RELIGIOUS PREJUDICE

PROFESSIONAL education and practice in all fields, including pharmacy, is not without its problems arising from this almost forbidden subject. The solution of this problem in the field of pharmacy is the same as that which must be used in meeting it on a broader scale.

One of the greatest difficulties is that many who profess to believe in democracy and the equality of opportunity promised by our Constitution and presumably practiced in this great nation give it only lip-service. Such persons are far more dangerous and detestable than those who are openly acknowledgely anti-Catholic, anti-Semitic or than those who widely proclaim their belief in "white supremacy."

It is almost dangerous today for one to speak out against religious and racial intolerance. One of the current devices used by those steeped in such bigotry is to label their adversaries as Communists on their program as Communist inspired. Actually it is such intolerance that makes our minority groups look with interest upon Communism wherein such artificial barriers are not recognized in spite of the system's many other faults.

The difficulty with man is that it is almost impossible for him to be objective, so much is he a product of his early training. From his earliest days he is taught to believe firmly and irrevocably the views of his parents and close associates in all matters pertaining to social problems. It is later only natural that he gravitates to that group wherein all members share his opinions and with such unanimity that his beliefs become even stronger until they assume the proportions of a divine revelation or even a directive from the Creator himself. Those few people whom he may meet and who may cast some shadow of doubt on his fixed ideas are dismissed as dangerous "crack-pots" who should be suppressed. All too often physical violence is used as a substitute for unavailable logic in combatting these dangerous heretics who question his views.

The battle against racial and religious prejudice is a difficult one. It is immediately apparent to one who thinks on this matter that those against whom prejudice is held by a majority can offer but slight resistance against it. As a minority group their protests fall on deaf ears and it is invariably construed as a plea of innocence by the guilty. The only hope of remedying this deplorable situation is by a steady effort on the part of those who are not oppressed to relieve those who are. Only those who are willing to bestow freedom and liberty on others deserve themselves its fruits and blessings.

If one be intellectually honest the following facts are inescapable and incontrovertible:

1. There is no superior race.
2. The alleged superiority of the white race is due to generations of better education, diet, environment and opportunity.
3. Given equal conditions, as above, no differences would be evident in a few generations in men of any color.
4. There are wide variations in individuals in intelligence and performance but these are not of racial origin.
5. A man's religion is in almost every instance what he was taught as a child. Rarely does freedom of choice play a part. There is, furthermore, no more valid justification for one religion than for another or for none since each is entirely a matter of belief not predicated on established fact and not subject to proof. This does not of course deny the constructive influence of religion in human affairs.
6. The freedom to worship God in any way without restraint is one of our liberties for which our forefathers fought and died.
7. The freedom to worship in any other way or even not at all must be just as inviolate.
8. The denial of opportunity or recognition because of one's religion or color is unscientific, undemocratic, intolerant, and contrary to the tenets of our Constitution.

Unless one can subscribe wholeheartedly to these stated truths and do so without wavering, it would be well for him to swallow his

resentment or anger and think with absolute honesty on the validity of these statements. Subjectively we may be convinced that to accept such a radical departure in our national conduct might hurt us personally but personal loss or gain should play no part in honest, objective reasoning.

It is of course true that there are individuals who are objectionable from many standpoints but there is no group along religious or racial lines that is exclusively so composed. Neither is there a group that is devoid of objectionable individuals. Democratic thinking and behavior does not fix as one of its requirements that we consider all men equal, for they surely are not. Rather it implies equal opportunity and then recognition of each individual based on achievement and personal attainment without regard for color or creed.

The time must come, and will come, when each man or woman is given equal opportunity in life without prejudice arising from sex, color or religion. Only then can achievement, or the lack of it, bring to each individual his proper measure of reward. Those who today are in the "select" group and who obstruct the accomplishment of this goal are courting disaster for themselves, their progeny and their nation. The suppressed people of the world outnumber the privileged by a tremendous margin and they no longer will listen to the promised benefits of democracy without its practice by those who profess it. There are many evidences in our country today that we intend to implement our democratic principles without fear or favor. To do so deserves every thinking man's support. To obstruct this policy is to risk a menace to our continued freedom and future far greater than any threat from without, actual or implied.

FOLIC ACID IN LIQUID PRESCRIPTIONS

By Stanley Scheindlin, M. Sc.*

FOLIC ACID became readily available in 1946, shortly after its synthesis was announced. At first manufacturers distributed this drug only in tablets, capsules, and injections. The retail pharmacist's only contact with folic acid was in the dispensing of these dosage forms.

Recently, however, an elixir of folic acid has been marketed and it is likely that, as time goes on, the pharmacist will have calls for folic acid combined with other drugs in liquid preparations. Experience with other members of the B complex, such as thiamin and riboflavin, has shown that these have often been prescribed in various liquid combinations of such nature that the activity of these vitamins has been reduced or destroyed. A widely known example is the prescription calling for both thiamin chloride and phenobarbital sodium. Depending on the pH of the final mixture, the result may be a dangerous precipitate of phenobarbital or precipitation and inactivation of the thiamin.

This study was undertaken in order to establish a foundation for the use of folic acid together with other prescription items. No previous reports on the pharmacy or compatibility of folic acid have appeared, but there is information on its chemical properties. Even before crystalline folic acid was isolated, Mitchell and Williams (1) reported the chemical properties of a highly purified concentrate. They stated that folic acid is unstable to oxidation, reduction, acid, alkali, dry heat, acylation, esterification, methylation, benzylation, nitrous acid, bromine, hypobromite, hydroxylamine, zinc dust and acetic acid (stable to acetic acid alone), and 1% hydrogen peroxide. In connection with studies on the folic acid content of foods, Cheldelin *et al.* (2) stated that the vitamin is unstable to light, but is not destroyed by autoclaving in the dark.

The synthesis of folic acid (pteroylglutamic acid) was first reported in 1945 by Angier *et al.* (3). Full details of the isolation, degradation, and synthesis of this dietary factor were revealed recently by essentially the same group of workers (4).

* Lederle Laboratories Research Fellow, Philadelphia College of Pharmacy and Science.

Folic acid is only very slightly soluble in water. Its sodium salt, however, is water-soluble.

Experimental

The folic acid used in these experiments was in the form of Folvite Elixir, supplied by Lederle Laboratories Division of American Cyanamid Company. This elixir contains 5 mg. folic acid per 4 cc. in a solution containing 10% alcohol, artificial red color, flavoring agents, and preservatives. The folic acid was present as the sodium salt, and the pH of the elixir was found to be 8.2.

Unless otherwise noted, all mixtures were stored in clear glass bottles on the table-top for the first week. They were thus exposed to electric light but not to direct sunlight. After a week the samples were transferred to a box where they were protected from light except when being examined. Mixtures were examined when prepared, after one day, one week, and one month. Any physical or chemical incompatibility was noted: *e. g.* precipitation, color change, liberation of gas, or change of pH. In order to detect any inactivation of the vitamin, additional samples of some of the mixtures were prepared and assayed for folic acid content.

1. Effect of Certain Organic Solvents

The effect of varying concentrations of alcohol, glycerin, and propylene glycol on Folvite Elixir was studied. Twenty-five cc. of the elixir were mixed with enough of the solvent and distilled water to yield 50 cc. of the desired concentration of the solvent. Mixtures containing the following concentrations of solvents were prepared:

Alcohol:	50, 45, 40, 35, 30, 25, 20, 15, 10, 5%	by volume
Glycerin:	50, 40, 30, 20, 10%	" "
Propylene Glycol:	50, 40, 30, 20, 10%	" "

None of these solutions showed any evidence of change after one month.

2. Effect of pH

A phosphates-citric acid buffer system was used, based on McIlvaine's buffers (5). Equal volumes of the buffer solution and the elixir were mixed.

pH of Buffer	pH of Mixture	pH of Buffer	pH of Mixture
10.9	10.3	5.9	5.9
10.0	9.6	4.8	5.1
9.2	8.5	3.8	4.1
8.0	8.0	2.9	3.2
6.7	6.7	1.9	2.4

At and below pH 4.1, immediate precipitation of folic acid took place. At pH 5.1, the mixture remained clear for over 24 hours, but at the end of a week some precipitation had taken place. No change was observed at any other pH, except that at pH 9.6 and higher, the red color of the solution was at first intensified, but had faded considerably at the end of a month. This was due to the coloring agent and not to the folic acid.

3. Effect of Various Prescription Ingredients

The following preparations were assayed for folic acid content after four months' storage at room temperature. The results are given in Table I. The column headed "Remarks" refers to the appearance of the solutions after one month.

Another group of preparations was assayed after being stored under different conditions. The results are given in Table II. The "Remarks" refer to observations after three months' storage at room temperature.

The precipitates that formed above could be resuspended easily on shaking.

These results show that sulfadiazine produced a striking inactivation of the folic acid. A non-competitive antagonism between folic acid and sulfonamides in bacteria whose growth is stimulated by folic acid has been reported by Lampen and Jones (6). These authors suggest that the synthesis of folic acid from *p*-aminobenzoic acid is the metabolic point at which sulfonamides attack these bacteria. Since such non-competitive antagonism has not been found in the case of *E. coli, S. aureus,* or *D. pneumoniae* it is believed that folic acid probably does not interfere with sulfonamide therapy against most organisms.

Significant inactivation of folic acid was also produced by Vi-Magna Syrup and Elixir Betalin Complex after three months, but after five weeks the bulk of the folic acid was still active.

TABLE I

Name and Amount of Medicant Added	*pH*	*Folic Acid (mg./4 cc.) Theory*	*Assay*	*% Folic Acid Recovered*	*Remarks*
None (Control)	8.2	5.4	5.76	106	Clear soln.
Alcohol 50%	9.0	2.7	2.3	85	Clear soln.*
Glycerin 50%	7.9	2.7	1.88	70	Clear soln.
Propylene Glycol 50%	8.2	2.7	2.44	90	Clear soln.
Phosphate Buffer pH 10.3	10.4	2.7	2.36	87	Color faded
Phosphate Buffer pH 5.9	6.1	2.7	2.4	89	Clear soln.
Compound Gentian Tincture 0.8cc./4 cc.	6.3	4.3	3.8	88	Clear soln.*
Wild Cherry Syrup 2 cc./4 cc.	5.9	2.7	2.28	84	Clear soln.*
Strychnine Sulfate 2 mg./4 cc.	7.9	4.8	5.2	108	Clear soln.
Phenobarbital Sodium 30 mg./4 cc.	8.4	4.8	3.9	81	Clear soln.
Methenamine 0.5 gm./4 cc.	8.6	3.78	4.24	112	Clear soln.
Aminoacetic Acid Elixir 2 cc./4 cc.	5.2	2.7	2.88	106	Ppt. formed within 1 week
Sodium Bromide 1 gm./4 cc.	7.7	2.7	2.42	90	Clear soln.
Ammonium Bromide 1 gm./4 cc.	6.4	2.7	2.3	85	Clear soln.*
Strontium Bromide 0.33 gm./4 cc.	7.7	4.8	5.1	106	Heavy ppt. within 1 day
Potassium Iodide 0.3 gm./4 cc.	8.0	4.2	3.64	87	Clear soln.
Ferric Ammonium Citrate 1 gm./4 cc.	6.5	2.7	2.8	104	Clear soln.
Sodium Nitrite 0.06 gm./4 cc.	7.6	5.2	5.8	111	Clear soln.
Fowler's Solution 0.2 cc./4 cc.	8.0	5.12	5.2	101	Clear soln.

*A slight precipitate or sediment formed *after* one month of storage. This is not an important consideration because prescriptions are usually used before this period.

TABLE II

Medicants Added	*pH*	*Folic Acid (mg./4 cc.)* *Theory*	*42° 5 weeks*	*% of theory*	*RT* 3 months*	*% of theory*	*Remarks*
Three Bromides Elixir	6.6	2.7	3.1	115	2.2	81	Slight ppt.
Phenobarbital Sodium	8.7	5.4	5.8	107	4.9	91	Clear
Sodium Bromide and Phenobarbital Elixir	6.7	3.8	4.2	110	4.4	116	Clear
Sodium Salicylate	7.0	5.4	5.2	96	4.0	74	Clear
Three Bromides Elixir and Phenobarbital	6.2	1.32	1.24	94	0.92	70	Slight ppt.
Elixir Betalin S (Lilly)	5.2	2.7	2.68	99	2.8	104	Clear
Elixir Betalin Complex (Lilly)	4.8	2.7	2.0	74	1.16	43	Slight ppt.
Sulfadiazine	7.2	5.4	1.2	22	0.25	4.6	Suspension
Vi-Magna Syrup (Lederle)	3.5	2.7	2.3	85	1.2	44	Separation of layers
Lederplex Oral (Lederle)	3.6	2.7	2.76	102	2.76	102	Separation of layers

*RT = room temperature.

In addition to the mixtures which were assayed for folic acid stability, other mixtures were prepared with the following results:

No. Name and Amount of Medicant Added	*Appearance After One Month*
1. Phenobarbital Elixir 2 cc./4 cc.	Clear soln.
2. Phenobarbital (in alcohol) 30 mg./4 cc.	Crystals deposited after one day
3. Chloral Hydrate 0.6 gm./4 cc.	Turbidity in 2 weeks; yellow ppt. in a month
4. Ferrous Sulfate 0.3 gm./4 cc.	Immediate precipitate
5. Ammonium Chloride 0.3 gm./4 cc.	Clear soln.
6. Potassium Thiocyanate 0.3 gm./4 cc.	Clear soln.
7. Antipyrine 0.3 gm./4 cc.	Clear soln.
8. Aminopyrine Elixir 2 cc./4 cc.	Clear soln.
9. Ephedrine Hydrochloride 25 mg./4 cc.	Clear soln.
10. Atropine Sulfate 0.5 mg./4 cc.	Clear soln.
11. Hyoscyamus Tincture 1 cc./4 cc.	Sediment in one day
12. Stramonium Tincture 0.75 cc./4 cc.	Sediment in one day
13. Nux Vomica Tincture 1 cc./4 cc.	Sediment in one day
14. Quinine Dihydrochloride 0.5 gm./4cc.	Crystals after one day
15. Ipecac Syrup 1 cc./4 cc.	Ppt. after one day
16. Cherry Syrup 2 cc./4 cc.	Ppt. in one hour
17. Raspberry Syrup 2 cc./4 cc.	Ppt. after one day
18. Ferrous Iodide Syrup 1 cc./4 cc.	Ppt. in one day
19. Acacia Mucilage 2 cc./4 cc.	Ppt. in one week
20. Calcium Chloride 0.5 gm./4 cc.	Ppt. in one day
21. Digitalis Tincture 1 cc./4 cc.	Slight sediment in one week
22. Compound Pepsin Elixir 2 cc./4 cc.	Ppt. in one day
23. Aromatic Cascara Sagrada Fldext. 2 cc./4 cc.	Compatible
24. Potassium Guaiacolsulfonate 0.3 gm./4 cc.	Clear soln.
25. Calcium Bromide—3 concentrations	Ppt. within two days
26. Potassium Acetate 1 gm./4 cc.	Compatible
27. Urea 1 gm./4 cc.	Clear solution

Remarks on the Incompatibilities

No. 2. The phenobarbital crystallized because there was not enough alcohol to keep it in solution.

No. 3. Chloral hydrate in solution decomposes into hydrochloric and formic acids (7) with a resultant lowering of pH. The pH of this prescription dropped from 7.4 to 4.7 in one month. The acidity precipitated the folic acid.

In Nos. 14, 16, 17, 18, 19, and 22 acidity was responsible for the precipitation.

Nos. 11, 12, 13, and 21 precipitated because insufficient alcohol was present to keep the plant extractives dissolved.

In Nos. 20 and 25 the calcium salt of folic acid probably precipitated.

4. The following products were mixed with equal portions of Folvite Elixir. Observations made after three days are noted.

Feosol Elixir (S. K. F. Co.)	heavy ppt.
Pentabromide Elixir (Lilly)	heavy ppt.
Metatone (Parke-Davis)	clear
Elixir Iron and Strychnine N. F. (Lilly)	heavy ppt.
Elixir Terpin Hydrate and Codeine N. F. (Lilly)	clear
Elixir Benzestrol (Schieffelin)	crystalline ppt.
Benadryl Elixir (Parke-Davis)	clear
Cheracol (Upjohn)	ppt.
Vi-Delta Oral (Lederle)	separation
Delphicol (Lederle)	ppt.
Solution Liver Extract Oral	clear
Elixir Ribothiron (Sharp and Dohme)	ppt.
Elixir Iron, Quinine, and Strychnine	ppt.

The precipitate in the mixture containing Pentabromide Elixir could not be redispersed by shaking. All the other mixtures where precipitation or separation occurred could easily be dispersed by shaking.

Conclusions

The prescriptions studied have been divided into three groups:

Group I

Mixtures in which no precipitate formed for at least one month, and in which the folic acid is stable for a reasonable period.

Group II

Mixtures in which a precipitate may form but which may be dispensed with a "Shake Well" label. The precipitate would be of a non-toxic nature and could be easily suspended by slight shaking.

Group III

Mixtures in which a precipitate formed, which could not be easily suspended or which contained a potent drug. These mixtures are not recommended.

Drugs which fall into these groups are:

Group I

Strychnine sulfate, phenobarbital sodium, methenamine, sodium bromide, ammonium bromide, potassium iodide, sodium nitrite, Fowler's solution, sodium bromide and phenobarbital elixir, sodium salicylate, elixir Betalin S (thiamin), ammonium chloride, potassium thiocyanate, antipyrine, elixir aminopyrine, ephedrine hydrochloride, atropine sulfate, fldext. cascara sagrada aromatic, potassium guaiacolsulfonate, potassium acetate, urea, compound gentian tincture, wild cherry syrup, ferric ammonium citrate, three bromides elixir.

Group II

Aminoacetic acid elixir, strontium bromide, ferrous sulfate, ipecac syrup, cherry syrup, raspberry syrup, ferrous iodide syrup, calcium chloride, calcium bromide, compound pepsin elixir, elixir Betalin complex, Vi-Magna syrup, Lederplex Oral, Feosol elixir, elixir iron quinine and strychnine, Cheracol, Vi-Delta oral, Delphicol, elixir iron and strychnine, Elixir Ribothiron.

Group III

Phenobarbital, chloral hydrate, hyoscyamus tincture, stramonium tincture, nux vomica tincture, digitalis tincture, quinine dihydrochloride.

Sulfadiazine was found to destroy folic acid activity very rapidly. The other prescription items that were compatible with the Elixir did not destroy the folic acid to any great degree within five weeks.

Acknowledgment

Acknowledgment is hereby made to Dr. Ivor Griffith for his counsel, and for his supervision of the conduct of this investigation.

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NEW SCIENTIFIC-MEDICAL TRENDS AND DEVELOPMENTS IN THE PHARMACEUTICAL INDUSTRY*

By Fredrick F. Yonkman, M. D.**

IN 1934 the Metropolitan Life Insurance Company published significant figures concerning the leading causes of death as they affect the population of the United States.

There is reason to believe that these ratios have not been altered appreciably.

Advances in medicine, and that means important progress in our field of activity, have followed accordingly. This progress of therapy has been presented in a different manner.

Rather recently the editor of the *Journal of the American Medical Association* asked several professors of medicine at leading universities in the States to list in the order of importance those medicaments which they deemed of greatest value. The consensus appears for 1945 and its comparison with that preference which prevailed in 1910 calls immediate attention to entirely new forms of therapy, thus indicating recent scientific and medical trends.

Man's chief enemy as Public Killer No. 1 is hypertension with its damaging effects on the heart, kidney and other organs. Your pharmaceutic industry has long been active in its attack on this most serious problem. Various industrial research laboratories have been cooperating with foundations, private and university medical investigators in such fundamental problems as the causes of hypertension. Simultaneously, varied efforts, some only partially successful, have been directed toward alleviating hypertension and its associated symptoms. We still seek the ideal agent whch affords relief in this disease. A hopeful and promising approach to the treatment of the neurogenic type of hypertension is that of attacking those predominating areas of the nervous system whose exaggerated functions may

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* Presented at the Annual Meeting of the American Pharmaceutical Manufacturers' Association, Havana, Cuba, April 14, 1948.

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lead to contraction of certain extensive beds of blood vessels, the result of which is an increase in blood pressure.

Pharmaceutic preparations now available still leave much to be desired in many instances, hence the necessity in the minds of many neurosurgeons of attacking this problem surgically.

Extensive sympathectomies, i. e. the cutting of involved pathways coursing through the sympathetic autonomic nervous system, are being performed daily, despite the fact that, at best, success is achieved by this procedure in only 35 to 40% of the patients thus treated. This percentage might be elevated by more extensive surgery or by still greater care in the rigid selection of candidates for such a mechanical attack.

A "medical scalpel," as Dr. Keith Grimson of Duke University confirms, is sorely needed. There are now available several agents which are capable of blocking certain functions of the autonomic nervous system, each with its own virtues and limitations. Among them one finds various derivatives of the ergot alkaloids and yobimbine, tetraethylammonium bromide and Priscol.

Although the latter are used in certain dyscrasias of the peripheral vascular system, they as yet have not earned their complete appraisal in the treatment of neurogenic hypertension. TEA (tetraethylammonium bromide) is probably too all-inclusive in suppressing autonomic functions, thus accounting for many of the side reactions which it produces. If its action could be targeted only toward the sympathetic ganglia and if a finely graded dosage could be established and maintained for such specific action, *controlled* depression of blood pressure could probably be attained. This goal may be difficult to achieve, however, with this type of compound. High hopes in this regard were held for a very potent compound called Dibenamine, but the detection of certain serious limitations during its clinical trial has thus far delayed its presentation to the profession at large.

Another agent cited is Priscol which has definite antisympathetic actions. It has been known in your country, in South America and on the Continent for its capacity to stimulate gastric secretion, but its chief virtue is that of relaxing spastic blood vessels such as occur in Raynaud's disease. This it does with relative safety, but what Priscol's eventual status as a blood pressure reducing drug will be is highly problematic. The development of this compound in laboratory and clinical research illustrates, in our opinion,

one of the rational approaches to this important problem of correcting or preventing vasospasm in various clinical conditions, including neurogenic hypertension.

Other new nonsurgical trends will become evident as those of us in research accept also the challenge of the surgeon who now severs the vagus nerves for gastric ulcer, the fifth cranial nerve for trifacial neuralgia or performs special surgery for those clinical conditions which might be treated more rationally on a medicinal basis.

Although cancer is not Public Enemy No. 1 in terms of man's chief lethal or incapacitating disease, it rates such a reputation in the public mind. Tremendous sums of money have been and are being expended in the attack on cancer and although one is inclined at times to be discouraged when reviewing the results, there is reason to hope that encouraging days lie ahead. As we tug and fight our way, struggling through the deep and extensive underbrush of the unknown, we have constantly in mind the thought that eventually Nature must give in by offering us certain clearings in reaching our final goal. Already we see certain new mileposts against the dim horizon.

The new nitrogen mustard compounds, drastic though they are in their violent action on tissues, have opened another field of real potentialities in the field of cancer therapy. Then too, the initial results reported on the use of certain relatives of folic acid, such as Teropterin, afford a faint gleam in this dark sky and we hope fondly for further confirmation in this regard. Especially promising are the encouraging results obtained with radioisotopes; significantly the use of radioactive iodine in the treatment of cancer of the thyroid affords a new avenue of attack on this and other forms of cancer. Further, the important clinical studies of Adair and Herrmann in New York, as well as of many others, point the finger to the possibilities of the male hormone, testosterone, in the treatment of cancer of the female breast, and probably in other forms of cancer. Just as intriguing is the use of estrogens in cancer of the male, particularly of the prostate gland. What metabolic mechansims are responsible for the favored results observed in some patients are problematic, but your research associates in the pharmaceutic industry are cooperating with various important investigative groups with the hope of finding some of the answers to questions posed. At present these studies, long conducted independently, are being

coordinated through the medium of the Therapeutic Trials Committee of the American Medical Association. This is a long range program which we trust will be ripe with important facts concerning the indications and contraindications of such hormonal therapy. And, before leaving this subject, we should like to repeat the query which we made in Augusta, Georgia in 1945. "Pneumonia, dysentery, septicemia and pyelitis may not always be prevented but they may frequently be arrested during the attack and aborted. Can we do the same with cancer? What can we find besides radium and x-ray which may safely complete or replace their lethal action on malignant tissue and do it so selectively that little, if any, accompanying damage is inflicted on surrounding healthy tissue? Is this too much to hope for? Who may yet find some antibiotic or enzymatic inhibitors to fill this bill? This may be only wishful thinking or an idle dream but it is a real challenge to investigators in our fields of activity."

Another common affliction is infection, the etiology of which is so varied. This wide latitude of causes makes more difficult the problem of successful prophylaxis or correction. The challenge is being met, however, and despite the fact that we still have far to go, we can all look back to the rather recent past and review the rapid development from Lister's antiseptic era of boiling, and of spraying carbolic acid around his surgical amphitheater, from iodine, bichloride of mercury, etc., to more specific chemotherapeutic agents like the arsenicals, sulfonamides and to the new current, dramatic antibiotic agents of the penicillin type. We have rapidly come a long way from Fleming and Florey's crude and toxic filtrates (which were homemade in flasks, bottles and enamel bedpans during war years) to our present form of sterile, pure, potent and nontoxic injectible preparations. And here one must doff one's hat to our confederates, especially the chemical engineers, in production for their successful efforts not only in supplying the demand but also in reducing the price of penicillin from its original level of $20 for 100,000 units in 1943 to 65 cents for the same amount today in the States.

Ingenuity has been exercised in the administration of penicillin in an effort to maintain an adequate concentration in the blood and body tissues while diminishing the frequency of injections. Penicillin in beeswax and in oils and gelatinous vehicles are noteworthy con-

tributions in this development. More recently there was the introduction of Caronamide by Sharp and Dohme which delays appreciably and safely the excretion of penicillin by the kidney. The latest innovation is that of a rather stable crystalline compound of procaine and penicillin G which, suspended in oil, affords a satisfactory preparation effective for twelve to twenty-four hours after a single injection. This type of compound can be dispensed in various viscous vehicles.

Similar advances have been made in regard to streptomycin with its special, potent and antituberculous action. Like penicillin the cost of manufacture is gradually dropping while the amounts being produced are increasing at the approximate rate of 300,000 grams per month. Of special interest is the fact that the bactericidal action of streptomycin can be considerably enhanced by an organic acid, *p*-aminosalicylic acid. This synergistic action should permit a marked reduction in the dosage of valuable streptomycin with probably a very significant decrease also in the frequency and severity of that serious side reaction of streptomycin, namely, damage to the eighth cranial nerve which, although rarely, may result in permanent deafness and severe loss of equilibrium.

Other synergists of streptomycin have been developed among which are those sulfones known as Promizole and Promin developed by the Parke Davis Research Staff. The experimental results regarding such combined therapy are encouraging and bear watching. Promin has already proved its primary value in leprosy. Here it is the drug of choice and it is responsible for the discharge of more patients than are admitted at the National Leprosarium at Carville, Louisiana!

There must be many other potent and relatively safe antibiotics available in natural resources. Among the many hundreds reported, one is encouraged to varying degrees by the reports on Bacitracin, Polymixin and also on Chloromycetin which is obtained from a soil fungus in Venezuela. Further study will eventually permit proper appraisal of *their* respective therapeutic advantages and such study should undoubtedly also afford us with other valuable antibiotics.

Much more should be said about specific chemotherapeutic agents in the treatment of malaria and other tropical diseases as well as various rickettsial diseases; one should emphasize the important

roles played by the newest insecticides and rodenticides as well as the newer anthelmintics in the prevention of this plague or that infestation. But, we must move along to other important items.

Man's most common complaint from a medical point of view is that of *pain*. Pain here and pain there! Even income taxes lead to headaches,—it all adds up to *pain*. Fine strides have been made in replacing morphine and other opiates by less expensive though equally effective synthetic substitutes which possess fewer undesirable side reactions.

We now have available Demerol and Methadon, each with special virtues. One of the newer discoveries includes certain piperidine derivatives, as reported from the Hoffmann-La Roche Laboratories. It is probably reasonable to anticipate with real assurance the development in the near future of several very active analgetic agents which possess few, insignificant side reactions.

Another common affliction of mankind is allergy in its numerous manifestations such as hay fever, urticaria, asthma, food or drug sensitivity, and others. On the assumption that histamine is released under certain conditions in the allergic patient, the logical investigative approach was in the direction of developing agents which would nullify the physiologic actions of histamine. Within a few short years intense activity in numerous research divisions has resulted in a formidable list of the so-called Antihistaminic Agents.

Each of these compounds has its special virtues and limitations. It must not be forgotten that these agents, valuable though they may be, are merely palliative and not curative. This vast problem of allergy merits the most serious attention through new avenues of approach, for example, from the point of view of either preventing the development of an allergy, or preventing the unleashing of histamine or other damaging factors during the allergic episode. Research is moving in these latter directions.

Your research enthusiasts have not been idle in the attack on certain blood dyscrasias, especially pernicious or primary anemia. The Lederle group demonstrated admirably the value of concentrated, coordinated research in striking while the iron is hot—they came up with folic acid with its dramatic capacity to improve the blood picture of certain anemic patients. But here, too, are further developments. It was soon learned by clinicians that folic acid had certain limitations,—it usually failed to improve the neurologic disturbances

of the patient afflicted with primary anemia; in fact, such disturbances frequently progressed to greater severity despite excellent improvement of the blood picture. Hence, the furious activity now being exercised in an effort to discover that "neural factor" which we know exists in the liver and in liver extracts.

Another important trend of interest is the search for new uses of existing preparations. One of the most satisfactory discoveries in this regard is that of Ochsner and Debaky of New Orleans; these clinicians successfully treated thrombophlebitis by injecting those sympathetic ganglia involved in the affected areas. Relief of pain released the spasm, thus permitting early recovery. Other examples include the use of curare as a supplement to modern anesthetics to produce complete muscular relaxation for surgery, of Tincture of Veratrum and magnesium sulfate in the treatment of eclampsia, of *p*-aminobenzoic acid in the treatment of certain rickettsial diseases, of urethane for certain malignancies; and so the list could be prolonged. This is indeed an important and challenging trend. One is tempted to predict that "relative to the numerous valuable therapeutic agents now on hand, there are probably just as many potentially valuable medicaments in Nature's storehouse and on the shelves of the organic chemist, if we only knew how to seek and test them, and to appraise them properly."

This discussion should not be closed without referring to the many safeguards established within and without our industry for the protection of the physician and his patient. Abundant experiences with the effect of a new drug in several species of animals are mandatory before the Food and Drug Administration of our government permits its introduction in the States, and similar referee boards function in a like manner elsewhere. We also have available the excellent facilities of the Council of Pharmacy and Chemistry and of the Therapeutic Trials Committee of the American Medical Association. Further, there are those special appraising committees associated with certain medical specialties such as the Committee on New Medicaments and Pharmaceutics of the American Academy of Allergy. All of these bodies offer their facilities to American pharmaceutic houses so that a new drug may receive very broad clinical scrutiny. Then too, many active and experimentally minded physicians in most fields of medicine are most eager to cooperate with the pharmaceutic organizations of good repute. The large facili-

ties of a well coordinated pharmaceutic research division is the answer to many a clinician's prayer. He knows that if his ideas are at all promising, he can anticipate excellent support and cooperation from the research staffs of the pharmaceutic industry. Thus, either through reputable groups or individual clinicians, a thorough study of a new drug is assured before the first prescription for that medicament is written.

Beyond these safeguards there stands that most important factor—the reputation of the pharmaceutic organization introducing a new product to the medical profession. That product must be right in every respect; a result of meticulous research, produced under the best of conditions, controlled zealously for potency, purity, and sterility, and promoted, in the most ethical sense,—these are the components which make the composite, that is, a good product, and the pharmaceutic industry jealously guards her excellent reputation.

And now, may we express again our sincere appreciation to our good Pan-American friends for their hospitality and cooperation. Together we have traveled as friends and we now look forward to new roads which stretch before us; may we continue to cooperate in full confidence and trust. Difficult days may lie ahead but such can serve only as a challenge. We would choose not to rest on our laurels but to accept such a challenge; in the words of Robert Louis Stevenson: "To travel hopefully is a better thing than to arrive, and the true success is to labour."

SCIENCE AND HEALTH OBJECTIVES*

By Austin Smith, M. D.

IN these days of seemingly endless drug miracles it is not difficult to become so engrossed in the specific actions of the drugs that sight is lost of the true purpose of medical treatment—which is not simply the cure of some infectious disease but rather the control of that disease to procure betterment of health of the individual and the improvement of the community in general. One tends too readily to think, choosing pneumonia as an example, of the lowering of the temperature and the quick recovery from an acute illness, rather than of saving a life, restoring normal health, and thereby providing continued usefulness of the individual and even economic security for him and his family. In turn, this relieves the community of a financial burden which it, or the state, would otherwise have to bear if the family were bereft of a provider or if he were incapacitated by the illness. These are important considerations and reflect the responsibilities that are assumed by those who manufacture and distribute drugs and by those who use drugs to prevent, diagnose or treat disease.

Thus, it would seem timely to reconsider what constitutes a health objective; how it may be attained; who participates; and the most effective method of approach. Such consideration may permit a better perspective of a contribution to humanity which is so extensive in scope that it may seem amazing to those who have not viewed it in its entirety. It is something concerning which all participants can take a real pride; in fact, there would be no censure if they experience some awe from their own achievements.

The objective of any health measure is to prolong lives and maintain usefulness, security and happiness. It makes no difference whether the measure is a new drug, a modified technic or an educational effort. Nor does it matter if it results from the efforts of an individual or a collective group; the important thing is the result, as appropriate credit inevitably is reflected, sooner or later. No matter who participates, or how—if the contribution is sig-

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nificant, everyone benefits. This is true regardless of the contribution: it may be a study of the diseases that are prevalent in an area; it may be the discovery of a new effective drug; it may be the determination of a better application of treatment; or it may be something less spectacular but equally important, such as the diagnosis of an individual case of a given disease, the control of a manufactured product, or the proper packaging or dispensing of a medicine for the patient. Each act, if it preserves the life of an individual, lessens his suffering or contributes to his security, or that of his community, is a reason for laying claim to personal achievement. Thus, the drug manufacturer, the physician, the pharmacist, the nurse—in fact, anyone who provides a true health service, can be assured of the importance of his or her help because it assists in making possible health objectives.

The attainment of any objective does not always rest upon the following of a routinely prescribed procedure. Often, the attack must be varied to meet the immediate needs. This is true of any attack. For example, the modern warfare observed in World War II called for modification, at times almost bewilderingly rapid, as new situations arose. So it is true for health warfare, which so far as combat and struggle are concerned, is far more complex than the mass attack observed when one nation sets upon another. Successful health warfare calls for the finest brains and the most intricate equipment, and, of great importance, understanding and sympathy as well as respect and admiration for other humans. It is the kind of warfare that gets results; that does good; that unites men in their efforts to advance humanitarian interests.

It is impossible in this brief period to list all who help in preserving health. But consider briefly the extent of some projects; such contemplation will provoke thought of many specialties and technics. Consider, for example, several phases of the control of malaria. Briefly, the problem is recognized as existing, diagnostic procedures are developed, new drugs are discovered, patients are treated, breeding places for mosquitos are destroyed by mechanical and chemical means, and the public is educated to the dangers of malaria and how to avoid it. Similar activities are involved in the control of tuberculosis, leprosy and other diseases that are known to South and North America. Not only are physicians, nurses, pharmacists and drug manufacturers involved, but also engineers, ad-

ministrators, chemical manufacturers, and all who are concerned with every procedure from clearing a swamp to putting proper labels on packaged goods. Every person who participates in any way in preventing disease, whether it be the use of drugs, the building of drainage canals, or the dissemination of health education literature, plays an important and respected role.

How best to gain a health objective is not always readily apparent. There is no pattern that can be cut for all health questions; it must be altered to fit the problem. However, there are a number of common principles that are almost invariably helpful, and some individual considerations that are specially useful for more than one project.

Medical education has extended far beyond its boundaries of even a decade ago. Today the person who makes full use of medical knowledge to which he is exposed, regardless of his special interests, is far better informed than were those of the preceding generation. In addition—and this is important—the general population is becoming increasingly aware of health hazards and of the possibilities that exist for maintenance of good health. Much of the latter has been brought about in devious ways: increased educational advances; health education in schools, clubs and elsewhere; lectures, posters, pamphlets and films; and deliberate attempts to bring together the interests of medical groups and those of the public. These are only a few of the ways that education has improved our lot; there are others of similar importance.

Of course, this information—for physician or other—has been made possible through research which has given rise to new ideas, new treatments, new preventive measures and new ways of putting them into effect. So much has been said about the virtues of research that there seems little need to belabor the subject on this occasion. But one phase that cannot be emphasized too strongly is the exchange of the information gained by experimentation. Without adequate exchange, the findings are of limited value. How this activity can best be brought about is in itself worthy of lengthy discussion and therefore it will have to be dismissed with a few words which I would like to use solely to emphasize how much can be gained by joint sessions between those with mutual interests. This meeting, for example, sets a pattern for discussions of international significance, and its importance in permitting people of the

great countries in the Americas to sit in friendly and helpful audience cannot be stressed too strongly. It is unfortunate that sometimes in the hurry of present day business we sometimes overlook the enjoyment and other blessings that can stem from neighborly relations. Furthermore, too frequently we forget how much information there may be available from sources other than those immediately at hand. I can think of many ways in which the people of the Americas are faced with similar problems and could benefit by mutual consideration of them. Published papers, joint scientific meetings, visits and interchange of trained personnel are only a few possibilities that immediately spring to mind. There are special facilities, interests and problems in each country and the help that can be provided in surgery, heart disease, endocrinology, infectious diseases, physiology, high altitude problems, and nutritional deficiencies—to mention just a few topics—would be of benefit to all participants regardless of their country and of whether they are physician or pharmaceutic manufacturer.

One of the ways in which it is possible for several or more groups to participate with mutual benefit is to engage in cooperative research projects, either by active research participation or by assisting in the underwriting of some basic work that must be done before new treatment can be devised but is too extensive for any one laboratory to undertake. For example, the Therapeutic Trials Committee of the American Medical Association's Council on Pharmacy and Chemistry is serving as a means of uniting the efforts of thirty-four investigating centers and thirteen manufacturers in the study of the effects of androgenic and estrogenic substances on cancer. This is an enormous undertaking, but it is indicative of what can be done on a voluntary basis and with mutual understanding and trust.

In addition, as another example, there has been proposed in the United States the creation of a foundation by the pharmaceutic and drug industry and the American Medical Association. The value of this proposal is obvious and needs no discussion at this time. It does, however, serve as further proof that when there is an opportunity for advancing our scientific knowledge, industry and the profession are quick to accept the challenge. In this instance, it is recognized that there is a great need for further information concerning aging of tissues, especially premature or abnormal aging,

and industry and medicine are determined, and rightly so, to do something about it. It is a tragedy to witness the rapid aging of someone in his thirties or forties when he should be capable of another thirty years of productivity.

Regardless of the nature of a health problem, it can be overcome if sufficient time and effort are devoted to it. Witness in the United States the increase in the life span—36 per cent in less than half a century; the decrease in tuberculosis—from first to sixth place within the same period; and the decline in malaria—at one time a vicious menace, now a feeble and rapidly vanishing foe. Other diseases can be similarly attacked, whether they are acute infections, malnutrition or leprosy.

At times it is impossible to predict where research will lead. The sulfonamides appeared because someone was interested in gaining better dyes for woolen goods; antibiotics are now in our medical armamentarium largely because an individual was interested in separating various bacteria in test tubes; and "promin" has gained recognition in the treatment of leprosy although at one time it was suggested for tuberculosis. This uncertainty, however, makes research all the more interesting and the outlook all the more hopeful for the conquering of diseases that still resist medical attack.

In spite of the advances that are made from day to day, there will never be a time when the world is free of disease. As one problem is solved, another arises; for example, as diseases of childhood and acute infections are overcome, and the life span extended, cancer and diseases of the heart and the blood vessels increase. This does not mean, however, that our health will not be better and our lives happier; this will happen, and more too. It does mean, though, that everyone of us who is interested in health will always have more than enough to do; we can rest assured that we will always be busy.

There is one phase of research that sometimes is overlooked and which at this time bears contemplation; it is concerned with the costs of medical care.

There are many who argue that the costs of medical care are increasing more rapidly than income, extending beyond the reach of a growing number of people. Of course, some of those who are most vociferous in advancing such statements have definite beliefs which they will advance regardless of what data exist. In fact, it

is not unusual for this highly vocal group to distort data to suit their whims.

To those who say unqualifiedly that medical care is increasing in cost, I reply it is not so if we take into consideration the increase in national income and the various factors that constitute medical care in its broadest scope during the lifetime of an average individual. And the pharmaceutic industry and the medical profession can be justly proud of their contributions. What are my reasons for refusing to admit unreservedly that the costs of medical care are continually increasing faster than income? There are several which I will present only very briefly as time does not permit details. But do not for one instant think that I am resorting to brevity to gloss over something that might not be defensible; there are facts for those who would seek them elsewhere.

No one will deny that food, supplies and general maintenance are much more expensive than in former years. Nor can anyone deny that the remunerations paid to supporting personnel are generally increased. Such items place an added burden on the cost of maintaining health centers. But these examples, which we will admit are not complete, do not completely embrace medical care as I visualize it; they represent only one phase, an acute phase, shall we say. Medical care if viewed in its proper perspective represents the care afforded an individual from the time he is born until he dies. To view it otherwise will result in a distorted picture and will encourage misrepresentation of medical facts pertaining to the individual. It is inaccurate to speak of the cost of medical care for that person during a period of illness when it may be the only illness for a period of many years or even during his lifetime.

Thus, if we are willing to admit the need for this broad viewpoint, we will find on examination that the individual now *gets more for his dollar spent in illness, spends a smaller portion of his income per year of life, and during a lifetime provides greater security for himself and his family with the dollars spent in medical care.* And this trend should continue.

To demonstrate the validity of the preceding statement we need study only a group of say 100 individuals. At the turn of the century they each had a life expectancy of roughly 49 years at birth. If they all contracted pneumonia for example, approximately thirty would die; the remainder would spend several weeks in bed at home or in

a hospital, followed by another long period of convalescence and part-time work. Today, such a group would have a life expectancy considerably in excess of 67 at birth and if the members contracted pneumonia, less than one per cent would die because of the availability of the sulfonamides and penicillin, while the rest would recover much more promptly with far fewer after-effects. In other words, there is a vast saving of lives and a marked reduction in time spent in illness, all brought about by a few cents' worth of drug, in addition to good medical and nursing care. The individuals in this group can be expected therefore to contribute many years of earnings to their own security, to that of their family, and to the community. The money value of a man to his dependents is increasing. The chances that a child will become an orphan are fewer today. Obviously, if the costs of medical care for pneumonia and the added expected earnings were pro-rated over the lifetime of any individual or of the group itself, it would be seen that the costs of medical care have not increased as rapidly as income but actually the costs are less, relative to ability to pay, than one or two decades ago. This should be a convincing argument for those who are willing to weigh both sides of any argument. For those who are biased and determined to foster their own views to the exclusion of all others, nothing can be done.

Other examples could be cited but, as I already have pointed out, this is not the time for details. Instead, it is best to consider the overall effect of medical science on health objectives and merely draw attention to a few of the problems that exist and the solutions that are available for those who honestly seek them. There can be no question about the members of this audience desiring answers to medical questions; all of us are vitally interested. Nor is there any question about the facilities and personnel that we have available in our countries in these western continents; they stand second to none.

There are, however, opportunities for further onslaughts on disease. These opportunities—or should I say challenges—must be seized quickly, promptly, and with every aid at our command. If this is done, the next time we meet in joint session like this, which I sincerely hope will be soon, we shall be able to discuss as accomplishments what today are dreams. But that is the way of all research—first the dream, then the deed. And that also is the way

of our peoples—they plan and then they act. Perhaps that explains in part the friendly relations that exist between the countries that are represented at this meeting. In any event, when groups such as this assemble it is always possible to close with the cheering note that no matter how much progress can be reported at this time, the next session will permit even more encouraging reports. I, like everyone else, am looking forward to that next session.

THE SCIENCE-SOCIETY COMPLEX

By John Lawson, B. A.

WHEN the technical developments of the past few years are subjected to thorough consideration, with a view toward their possible implications, and are compared with the influences of previous scientific progress on the past advance of civilization, the existence of an acute problem becomes apparent. How can the enormous potentialities of science and its newer products be appropriately fitted into the framework of modern society for the improvement of world culture? Science and society must discover a common meeting ground and scholars and educators now are beginning to propose generalities and theories to form a background for the future mechanics that will have to be devised to solve this imperative question in the best interests of mankind. Future events will testify whether this confusing conflict is being accorded sufficient attention by both science and society. To what extent the difficulty is being cogitated will be sketched hereinafter. At the present time, science requires more critical evaluation of its widespread applications, but constructive criticism is impossible without a better public understanding of the true philosophy of science.

Public Understanding of Science

In emphasizing this currently urgent necessity, Professor Herbert Dingle, in his 1947 inaugural lecture at University College, London, said that science has had "no need of standards of judgment, and so has produced no critical school, but by this it has lost the other and greater benefit which such a school can give—namely, that of surveying, describing and interpreting the movement itself. That is why it can combine with such brilliancy of achievement such obscurity of understanding." In this country, unversities are beginning to integrate more closely their teachings of the sciences and the liberal arts. Yale has reorganized its scientific curriculum and Harvard has instituted a lecture course to explain the sciences to nonscientific students. In fact, Dr. James Conant's book, *On Understanding Science,* has deeply impressed many college officials. The logic of an intimate alliance between the sciences and that which Yale calls the humanities is further manifested if one agrees with the definition in Dr. Douglas F. Hill's book, *Science.* He believes

it "to mean the power to think logically, dispassionately, impersonally, objectively and thoroughly according to a definite pattern that can be consciously adopted and taught; to extend knowledge by ordered experiment; and perhaps . . . to act fearlessly in the conclusions reached."

The problem is many-sided and each facet has its individual ramifications because current thinking thus far has attained merely the stage of offering hypotheses upon which a solution may be constructed. Nevertheless, certain considerations appear basic and are presented for two primary reasons: to underscore the complexities which merit regard and to point out some fundamental observations which furnish a basis for a rational approach to the eventual formation of a practical relationship between science and people. The results of war research brought science into sharper focus for people, and society now faces the difficulty of learning to appreciate scientific work and to use it properly. President Truman's Steelman Report and the debate on a National Science Foundation, for example, are evidence that public consciousness is being stimulated. This warrants increased development by means of improved education and guidance. Ralph H. Ojemann, (1) of the State University of Iowa, writing in *Science* magazine, advocates three specific changes in the dissemination of scientific knowledge. It should include a description of the intricate methods by which findings are discovered so that the disappointments, determination, zeal, cost, and other characteristics of technical investigation will be comprehended. It should be altered to help students to know the probabilities of error in experimentation and the extent to which a course of action can be planned. It should be modified to emphasize consistently that scientific knowledge is constantly changing and that factual vacancies must be filled as information is acquired. These measures, Ojemann believes, will serve to better public awareness of the significance of science. As he asserts, "Thus, it appears that, with present methods of educating and guiding youth and adults, the basic appreciation of the scientific approach is not especially well developed. . . . If all the various dissemination media, including textbooks, newspaper and magazine features, motion picture reports, and radio presentations will give more attention to the basic concepts involved, the job may be done before the lessons of the war recede too far in popular thinking."

Scientific Appreciation of Society

While people are studying science for a richer comprehension of its activities, science would do well to scrutinize society to discover how human behavior patterns may be expected and influenced to act in response to technical advances. As a student of this phase of the situation, Douglas G. Haring, (2) of Syracuse University, points out that the possibilities for prophesying cultural behavior in relation to customary activities are generally good. Although everyone's unique heritage is his individuality, predictable response usually is a reflection of past experience. However, Haring makes the commendably bold proposal that perhaps behavior patterns, as they now are known, should in some way be obsoleted, because they do not permit observers to contemplate human reaction to scientific progress, and the latter cannot be interrupted. Indeed the improvement of society's adaptability depends on technical successes just as surely as the advances of research are contingent upon society's appreciation of the classical meaning of science. Their interdependence calls for a uniform acceleration rate for the progress of society and science, and a competitive race is strongly contraindicated. An immediate cure for this challenging disorder may not now be at hand, but the Syracuse official's succinct conclusion constitutes thinking in a logical direction. His plea for scientific understanding of social phenomena is eloquent: "Evolution is irreversible; social living is sequence and the past cannot be recreated. If new social inventions are to solve the problem, they will occur if and when research provides the requisite knowledge and insight. The general acceptance of such innovations, however, is another matter and cannot be predicted. The human species may prefer blind adherence to traditional societal patterns despite impending extermination." In this acute puzzle which is the theme of this writing, acceptance and adherence are two of the fine points that require science's precise assay and society's determined appraisal.

Realistic Aspects: Adaptation and Atomic Politics

It was previously noted that a long-range view of the problem presented by the society-science complex must necessarily be cloaked to some extent, at this stage of its growth, in hypothetical generalities. But a few specific aspects of the situation may be analysed in the present, and certain proposals and currently pursued fields of

activity have a relation to the matter. These are of a significance that permits optimism for future clarification, provided they are appropriately conducted. At the same time, scientists are being cautiously realistic in their advice on how this new scientific thinking might be applied to economic and social possibilities of the near future, basing their suggestions on their observance of the difficulties that had to be surmounted by past progress. When Waldemar Kaempffert, (3) Science Editor of *The New York Times,* and an eminent scholar of modern technology, addressed the 1947 graduates of the Philadelphia College of Pharmacy and Science, he noted a need for adjusting society to the speed of science. Changes in modes of travel, dress, living, working, etc., have been continuous in the past and people have benefited. The future will see greater changes and call for greater adaptation. Kaempffert foresees disposable suits of clothes, thermoelectric power, and synthetic meals as examples of radical probabilities. The confusion that must result from changes and that must be overcome by adaptation is typified by contemplating acclimation to these future scenes, and moreover by the chaotic inferences of atomic energy, unless applied for constructive purposes. In this case a solution may lie in peaceful world-wide relations plus international research.

More specifically, frictionless atomic politics, according to Leo Kartman, (4) of the University of Hawaii, requires that science participate in governmental administration for three reasons. (a) Since nationalism may be unable to cope with the atomic potential, the greater proportions of international scientific co-operation may prove to possess this capacity. Kartman believes that "the control of atomic energy by the United Nations is both feasible and necessary. We cannot base ourselves upon the abstract formulation of nationalism *versus* internationalism even though atomic power emphasizes the theoretical validity of this contradiction. The problem of the world control of atomic energy must be given the practical task of purging nationalism of its militaristic side and strengthening those scientific elements within it which will orient a foreign policy on the basis of the peacetime use of atomic power. This is the first precondition for world co-operation which may entertain the idea of ultimate federation within the purview of its political philosophy." (b) Science must take a political stand in the feud between the colonial countries and western industry to demonstrate that the

former would be benefited by the application of nuclear power to industry. (c) Science, with its atomic-ace-in-the-hole, is in a position to dispel the old-fashioned scientific attitude (which has prevented scientists from applying the achievements of their craft to political thinking) and to influence the United Nations to follow their intended course. Conceivably this position also is appropriate for disproving the inevitability of war, at least for several generations.

Science and the Nation

Since this examination of the society-science conflict thus far has been made in an effort to reveal some of the broad and a few of the specific aspects of the problem on a world-wide and general basis, it seems in order now to visualize a part science is playing and could take in the national picture. It is unfortunate that a war appears to be necessary to stimulate science to great accomplishments, but history confirms this premise. As a result of wartime production records, the nation has a new realization of its industrial resources. When Marshall H. Stone, (5) of the University of Chicago, retired as vice-president of Section A of the American Association for the Advancement of Science, he observed, "The war confronted us with at least two major problems which made extremely heavy demands upon our knowledge in this domain [production]: that of managing our own productive processes with maximal efficiency in relation to our total wartime requirements, and that of throttling those of our enemies in the most effective possible way with the means at our disposal, especially by strategic bombing and by submarine warfare. I believe that the experience gained in working with these wartime problems, with their definitely military character, can be used to guide our study of production under peacetime conditions for peacetime needs."

Government leaders at the national level, too, recognize the increasing need for scientific opinion in matters affecting the administration of society, and science is emerging from its realm of reticence to assist in the evaluation of economic theories and to contribute to the development of a more realistic public management, or a benefited statecraft, as Dr. Stone terms it. Statecraft requires organized teams for facilitating the adjustment between theory and practice. Collaboration and weighing of essential considerations has begun. As Dr. Stone reports, "The recently formed Atomic Energy Commission is, no doubt, primarily intended to provide for a properly

safeguarded engineering development of atomic power, but it will obviously have to consider many questions which fall within the domain of the social sciences. It seems to me important that similar attention should be given to the social effects of the many other innovations flowing in an ever-widening stream from our laboratories."

Whether current national legislation is a product of crystallized ideas on the society-science question and its elaborate implications, is conjectural, but Federal laws have been enacted which should serve to ally science and politics, even though this alliance may not have been initially intended as a major reason for their passage. William Vogt, (6) War Department consultant on scientific, educational, and cultural affairs, points out long-range possibilties inherent in the Fullbright Law amending the Surplus Property Act of 1944. This authorizes the State Department to dispose of United States property located outside the U. S. in exchange for the tuition of foreign students in American schools located in foreign countries. The cultural and scientific interchanges thus provided offer freedom of international communication by way of the universal tongue of science. Ornithologist Vogt writes, "Men have been united by science since the time of the Renaissance, and political internationalism can learn much from the scientific pattern." All countries stand to benefit from a deeper understanding of each other's technical philosophies and limitations, and science stands to profit provided it can exert its influential qualities along correct lines. Future legislation may reflect a growing cognizance of the capacities of science that fit into the social forces of politics and economics.

For the Future

Although there appears to exist, as heretofore surveyed, a maladjustment between science and society as underscored by various observations and suggested primary remedies, the fact remains that progress to date supports the rationality of optimism for the future. Charles F. Kettering, (7) Research Director of the General Motors Corporation, when he retired as president of the American Association for the Advancement of Science, asserted that each wartime miracle was possible because of freely accumulated knowledge, and that the wonders of radar, penicillin, DDT, jet propulsion, high-octane fuels, and atomic power were developed over long periods of time. In tribute to the less obvious factors of industrial success

that sustain the logic of hope for an optimistic posterity, he stated, "We often hear people express their gratitude for America's natural endowments—its resources of coal, oil, minerals, land, and timber. The backlog of scientific knowledge, our mass-production facilities, our technical societies, and our educational system are rarely considered as resources, yet we know that without them we could never have reached the position we occupy today among the nations of the world." The validity of unbridled enterprise and of boundless thinking is upheld by contrasting the basic morals which divide authoritarian ideology and democracy. The latter encourages advances as produced by change, subject to open-minded criticism; the former inhibits it. This open-mindedness is a vital requisite for a mutual appreciation between science and society so that each may be exploited for the benefit of the other and for the good of man's march for improvement.

Conclusion

Any discourse projected to summarize current thinking on the disagreement between technology and culture must necessarily be nebulous and in general limited to the phase of theory because the conflict is relatively young. At the same time, certain observations and proposable conclusions are within our scope. When society and science learn to appreciate each other's difficulties, the essential, common meeting ground will come into focus. Colleges are doing their part. Changes and adaptations are mandatory. Reticence should be abandoned for the sake of increased indulgence by science in national and international politics. That which has been done so far is reason for optimism, provided the means can be discovered to facilitate co-operation and cause it to become increasingly imaginative and intensified.

In addition to pursuing our customary course of democratic freedom so that the mechanics for solving this science-society complex may be developed on a flexible basis to fit the changing times, a pessimistic view of the future is repudiated when a justification for present conditions is found. Lecomte du Noüy supplies a somewhat surprising justification and an idealistic remedy in his widely heralded book *Human Destiny*. By taking an extremely long-range look, and tracing evolution from the beginning, he predicts the ultimate existence of possibly a superior race. Man is the approach to this goal and if he didn't have difficulties to overcome, evolution

would cease. Dr. du Noüy is convincing in the adroitness with which he pleads for a return to religion as a potent, modern prescription not only to ameliorate international cross-purposes, but also to alleviate the conflict between the philosophies of human nature and its fields of activity. Man and his science are here to stay. True scientists recognize that all life cannot be explained on a scientific basis, yet to some extent, science is responsible for the fact that theology has lost its grasp on society, because the greater part of life may be accounted for by mere scientific principle. Man has lost sight of the part that cannot be thus explained. Current thinking and rationalizing contribute to that which is to come, and after trial and error, progress and problems, barriers and pitfalls, all witnessing scientific and social progress, the final rendezvous, perhaps centuries hence, may be a life in which religion is modernized with civilization.

Our present-day advancement considered in all its various aspects, cannot fail to be instrumental, in one way or another, in the search for the goal, and perhaps co-operation between society and science would be made less complex if both were to seek a common tongue. To satisfy both, the language of the supernatural appears revolutionary but nevertheless not illogical, particularly should simpler compromise forces prove futile. Indeed a more universal form of expression among human fields of endeavor, and parenthetically among nations, is the imperative desire of our time. The opportunity for improved co-ordination between people and their activities is evident, and the means for realizing it are not unavailable so long as the search continues to be constant and the ideal remains humane and clearly defined.

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SUGAR-COATING THE FURNITURE FOR BETTER WEAR

By T. Swann Harding

WELL, scientists think of about everything, if you only give them time enough. Now they have succeeded in preparing an excellent lacquer or varnish from starch or from ordinary sugar-bowl sugar. Pretty soon you may find on the market an exceptionally durable finish for wood and metal which will withstand the burn of a lighted cigarette without even wincing. How did all this come about? Since the chemists started on starch, suppose we start there too.

The starch made in this country is prepared from corn, potatoes, or wheat, but a great deal of tapioca starch is imported for special uses. Much of all of this starch is used for food; however, a billion and a half pounds of it finds its way into industry. Prominent among industrial uses are the sizing of paper and textiles, the making of adhesives, and the finishing of wearing apparel and household fabrics in those institutions known to wags as dissolving plants, but to their proprietors as laundries.

When starch is heated, its composition and its properties change rapidly and considerably. When acid is added, crystalline dextrose—glucose, or "corn sugar"—is produced. However odd it may seem to some, chemists regard starch as an alcohol, for it has all the chemical reactions characteristic of an alcohol, and in these reactions important starch derivatives are produced. In this way starch loses its familiar aspects and acquires altogether new characteristics. Oddly enough only one starch derivative so far prepared has found practical use and that is starch nitrate, an explosive!

Since starch, like table sugar, is an alcohol, it has a corresponding ether or so. This, in a manner of speaking, is a starch oxide. One of these, the allyl ether, is prepared by the action on starch of a petroleum byproduct called allyl chloride. As originally prepared it is a soft, gummy, but not tacky substance which, when left exposed to the air, becomes coated with a hard, insoluble material. This allyl starch has some extremely interesting properties when in the form of a thin film.

To get it that way it is dissolved in the ordinary lacquer solvents in which form it can be brushed or sprayed on as a protective as well as decorative coating for wood, metal, glass or other surfaces. When the film dries and hardens it has marked durability, great resistance to heat and to abrasion, and high resistance to acids, alkalies, and other chemicals, including those which dissolve it readily in its original unhardened form. This suggested its use as a lacquer or varnish for household and office furniture, and for numerous other articles.

Manufacturing concerns immediately became interested. But the first process devised for making allyl starch was inefficient. However the improved process, using allyl chloride, removed that obstacle. Moreover the costs of the raw materials are now reasonably low. But the curiosity of a chemist is something that far exceeds that of the proverbial woman. Was allyl starch the last word, or could something better be made?

True, a piece of wood finished with allyl starch bears up nobly under the impact of a lighted cigarette, which badly burns exactly the same kind of wood covered with ordinary commercial finishes. It easily withstands temperatures up to 400 degrees Fahrenheit. Alcohol, gasoline, or other liquids, cocktails included, can be spilled on an allyl-starch-coated table top without leaving marks or injuring the surface. Hot dishes leave no marks.

What is more, solutions of allyl starch can be used to impregnate wood, paper, and textiles, rendering them more wear-resistant, increasing their strength, and making them invulnerable to many reagents. The material can be used as an intermediate in making plastics. Gummy allyl starch can be modified by mixing with it substances commonly used to vulcanize rubber—sulfur, for instance. When such mixtures are heated under pressure a rigid material is produced that is highly resistant to heat and to chemical reagents.

Finally allyl starch has good adhesive properties. By its use laminated products of good strength and quality can be prepared from wood, paper, or fabrics, by coating sheets of these materials and then subjecting them to heat and pressure to fix the coating. It makes excellent stickum for veneering.

But starch is not the only carbohydrate. There are, of course, a whole group of sugars, all of them alcohols, many varying in chemical composition. They vary also in other properties, some

being sweeter than table sugar, others scarcely sweet at all, and at least one of them having a bitter taste. They are all alcohols, hence the chemists made a lot of their allyl derivatives to see what they would be like.

Ordinary table sugar has few industrial uses other than in the fermentation, baked-goods, and candy lines. The only derivative of this sugar which has been made even on limited industrial scale is sucrose octaacetate. This material is used as a plasticizer, as an ingredient of lacquers and adhesives and for denaturing alcohol.

Naturally, since table sugar is an alcohol—be careful how you tell Uncle Dick about that—an allyl sugar or allyl sucrose can be prepared from it. Quite recently this has been done by the same group of research workers in the U. S. Department of Agriculture's Eastern Regional Research Laboratory (near Philadelphia) which did the above-described work on allyl starch. These workers did not overlook an important fact that appears to have been ignored by previous workers who prepared allyl sucrose, i. e. that coats of it would change into highly protective, insoluble and infusible films.

As prepared, allyl sucrose is a heavy light-yellow liquid. When it is exposed to air, particularly at elevated temperatures, it undergoes a series of changes and finally hardens into an insoluble, infusible, transparent resin. In the language of the chemist it polymerizes—i. e. bigger molecules are made out of smaller ones. Cobalt naphthenate was found very effective in helping this process along.

The nature of polymerized allyl sucrose made it immediately evident that the material would prove extremely valuable for coating wood, metal, and other surfaces which might be subject to the action of solvents, oils, abrasives, or heat. While the sirupy allyl sucrose is quite soluble in almost all common organic solvents, a properly cured film of the material is not only insoluble in them, but it will withstand immersion in hot oils and resists heat up to 200 degrees Centigrade.

Moreover the coating possesses high gloss, extreme hardness, and sufficient flexibility to improve its desirability still further. Like allyl starch, allyl sucrose may also be modified with various plasticizers and other resins. It also has good adhesive properties and, since it is transparent, it would serve to make plates of glass adhere to one another. It also would make an admirable waterproof ad-

hesive for laminates; it can be used to coat and impregnate paper, textiles, and other materials, water- and greaseproofing them, and improving their strength.

Not only does an entire new field of industrial usefulness for ordinary cane or beet sugar open up here, but other derivatives of sucrose may prove equally interesting and valuable. Furthermore quite a new field opens in the manufacture of highly resistant and very decorative lacquers, varnishes, and plastics.

Desk tops and table tops may be coated with these new materials, allyl starch and allyl sucrose, and display phenomenal resistance to the common forms of abuse to which such articles are ordinarily subjected by free American citizens—especially when said articles belong to other people. The coatings are highly decorative in addition; they bring out or accentuate the grain design of the wood. Allyl sucrose coatings more closely resemble enamel than they do lacquer or varnish.

Then similar materials may be prepared from a large number of other sugars and carbohydrates—most of which laymen do not even know by name—but any one of which may yield a substance especially appropriate to some specific uses. All behave somewhat like allyl starch and allyl sucrose. They are easily miscible with one another, hence blends can be made, rendering it possible to produce coatings of various degrees of hardness, adhesiveness, or penetrating power, as desired, while resistance to solvents and to heat can be tailored to specifications.

SELECTED ABSTRACTS

The Spinal Anaesthetic Effects of Ephedrine Sulfate: A Preliminary Report. J. E. Ruben, P. M. Kamsler and W. L. Howell, Jr. *Science 107,* 223 (1948). Although the addition of ephedrine to spinal anaesthetic mixtures for the purpose of prolonging the effect of the latter is now practiced rather commonly, the only published report on the spinal anaesthetic effect of ephedrine deals with an investigation performed on frogs.

This paper is a preliminary report of the observations made on 15 patients, each of whom received a subdural injection of 50 mg. of ephedrine sulfate in triple-distilled water mixed with 1 cc. of spinal fluid. All of the patients showed some diminution of pin prick sensation varying from slight hypesthesia to anaesthesia; diminution of anal sphincter tone was also noted. Effects were usually noted after ten minutes or more.

No elevation of pulse or blood pressure was observed. A number of the patients experienced the warming of the lower extremities associated with lumbar sympathetic nerve paralysis, and a few cases exhibited the drop of blood pressure often seen in spinal anaesthesia. In some cases ephedrine anaesthesia sufficed for surgery, no other standard anaesthetic agent being employed.

The authors advise that the anaesthetic effect of ephedrine should be considered when this drug is to be added to spinal anaesthetic mixtures.

Absorbable Hemostatics: Their Uses and Identification. J. W. Fairbairn and T. D. W. Whittet. *Pharm. J. 106,* 149 (1948). The authors review the sources, uses, microscopical characters and tests for identity of the absorbable hemostatic dressings fibrin foam, oxidized cellulose, gelatin sponge and calcium alginate. The first three were developed in the United States; the fourth, in England.

Fibrin Foam. This substance, prepared from fibrinogen and thrombin, has been extensively tested and appears to be safe and efficacious. When used in surgery of the peritoneal cavity, abdominal wall, kidney, lung and liver, it is said to be absorbed in about five weeks. Its method of use requires the addition of freshly prepared thrombin, and sterilization is accomplished by a special procedure.

Oxidized Cellulose ("Oxycel," Parke, Davis & Co.). This is prepared from surgical gauze or cotton by an oxidation process in which cellulose is converted into polyanhydroglycuronic acid. Oxidized cellulose resembles the parent material in texture, but is more pliable and easier to pack into wounds. Upon becoming wet with blood it becomes slightly sticky and swells, forming a dark brown gelatinous mass. It is contra-indicated when penicillin treatment is employed, since it inactivates this antibiotic. Oxidized cellulose is stated to delay bone repair. Sterilization must be performed by chemical means, since heat cannot be used.

Gelatin Sponge ("Gelfoam"). This occurs as flat rectangular pieces, about 9 cm. x 12 cm. x 1 cm., of white color, extremely light weight, and a porous fracture. It consists of whipped or foamed gelatin; it may be cut with scissors and retains its tensile strength on wetting. This material does not inactivate penicillin, and it may be used either with or without thrombin. Gelatin sponge may be sterilized by dry heat, but autoclaving destroys its physical properties.

The authors quote Pilcher and Meacham as preferring gelatin sponge to fibrin foam because of its easier application. Their conclusions were drawn from a series of neurosurgical operations in which 272 cases were treated with gelatin sponge and 115 with fibrin foam. Jenkins and Clarke have reported an occasional inflammatory reaction to the sponge, resulting in early liquefaction.

Calcium Alginate. This material has not been subjected to thorough clinical tests, although preliminary reports have appeared on it. It is prepared from alginates obtained from Scottish seaweeds; when sodium alginate solution comes into contact with a calcium salt, a coagulation occurs which makes possible the preparation of hemostatic foams, filaments, cloth, gauze, wool, or a film resembling Cellophane.

It possesses the advantage of withstanding autoclaving without serious loss of physical properties, and it is also compatible with penicillin.

A comparison is furnished of calcium alginate gauze and oxidized cellulose gauze as to microscopical appearance and behavior when subjected to chemo-microscopical tests. Test tube reactions for differentiating these materials from each other and from cotton are also described.

Test tube reactions of gelatin sponge and fibrin foam are reported.

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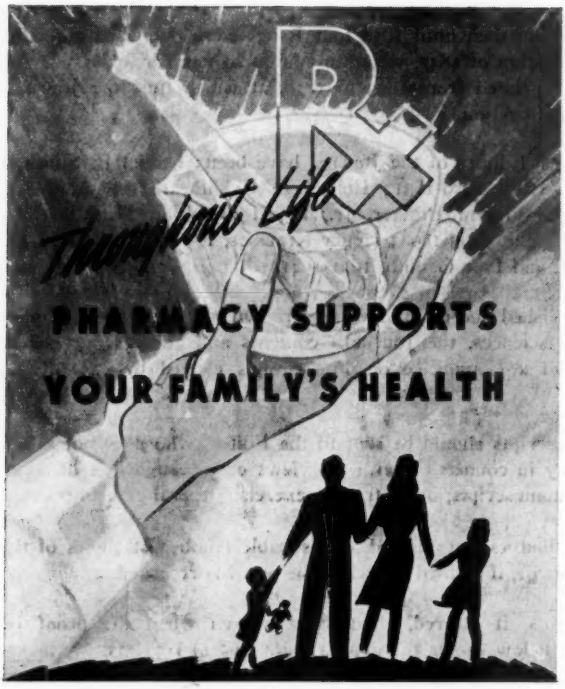
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